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(12) **United States Patent**  
**Dixit et al.**(10) **Patent No.: US 6,586,206 B1**  
(45) **Date of Patent: Jul. 1, 2003**(54) **METHODS FOR MAKING RECOMBINANT PROTEINS USING APOPTOSIS INHIBITORS**(75) Inventors: **Vishva Dixit**, Los Altos Hills, CA (US);  
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(51) **Int. Cl.**<sup>7</sup> ..... **C12P 21/00**; C12N 5/10;  
C12N 15/87(52) **U.S. Cl.** ..... **435/69.1**; 435/69.2; 435/325;  
435/358; 435/465(58) **Field of Search** ..... 435/69.1, 69.2,  
435/325, 358, 465; 935/33, 44(56) **References Cited****U.S. PATENT DOCUMENTS**

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(List continued on next page.)

*Primary Examiner*—Gabrielle Bugaisky(74) *Attorney, Agent, or Firm*—Diane L. Marschang(57) **ABSTRACT**

The invention provided improved methods of making and producing recombinant proteins in in vitro cultures of host cells using apoptosis inhibitors. The use of one or more apoptosis inhibitors in the methods can reduce apoptosis in the cell cultures and markedly improve yield of the desired recombinant proteins.

**21 Claims, 15 Drawing Sheets**